REMARKS

The Final Office action sent July 9, 2008 has been received and reviewed. All claims stand rejected. The application is to be amended as previously set forth. Support for the amendments and new claim may be found throughout the as-filed Specification, for example, in at least Example 4; page 12, lines 26-33; page 13, lines 1-25; Figures 3 and 4, and the claims as previously presented. Accordingly, applicants submit no new matter has been added. The withdrawal of previous rejections is noted with appreciation. Reconsideration is respectfully requested.

35 U.S.C. § 103

1. Claims 1-3 and 7 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Farnsworth et al. (Canadian J. of Comp. Med., July 1975, (39): 340-348; hereinafter 'Farnsworth') in view of Lohuis et al. (J. Dairy Sci., 1989 (72): 75-98; hereinafter 'Lohuis'). Applicants respectfully traverse the rejection as follows.

Applicants submit that none of references relied upon by the Examiner, when combined and/or considered as a whole, teaches or suggests a composition as presently claimed, to wit, comprising, both at least 20mg of prednisolone and an anti-bacterial agent. Furthermore, the unexpected results obtained by applicants' claimed composition constitute evidence of the non-obviousness of applicants' claimed composition. That being said, in order to expedite prosecution of the instant application, claim 1 has been amended to recite, in part,

> "said pharmaceutical composition providing increased anti-inflammatory efficacy while not increasing immunosuppressive side effects in the non-human mammal, wherein the composition comprises: an antibacterial agent, prednisolone, and a pharmaceutically acceptable carrier... wherein the increased anti-inflammatory efficacy while not increasing immunosuppressive side effects may be determined by displaying a similar leukocyte count upon administration to the non-human mammal when administered intramammarily, as compared to the non-human mammal to whom the pharmaceutical composition has not been thus administered."

To establish a *prima facie* case of obviousness, the prior art itself or "the inferences and creative steps that a person of ordinary skill in the art would [have] employ[ed]" at the time of the invention are to have taught or suggested the claim elements. Additionally, there must have

been "a reason that would have prompted a person of ordinary skill in the relevant field to combine the [prior art] elements" in the manner claimed. *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1742, 167 L.Ed.2d 705, 75 USLW 4289, 82 USPQ2d 1385 (2007). Furthermore, applicants note that a greater than expected result or the presence of an unexpected property is evidence of nonobviousness. *See, e.g.,* MPEP § 2144.05, emphasis added.

The Examiner alleges that the teachings of Farnsworth and Lohuis would have motivated a skilled artisan to vary the concentration and to try 40 mg of prednisolone in order to see the effects on the immune cells. Final Office Action at page 4. Applicants note that whether or not it would have been obvious for a skilled artisan to vary the concentration depends upon whether that skilled artisan is choosing from a finite number of identified predictable solutions, with a reasonable expectation of success. *See, e.g.,* MPEP § 2145 (X) (B) citing *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1397 (2007). Applicants submit that the unexpected results and evidence of record suggests that there would not have been predictable number finite solutions, and that would not have been a reasonable expectation of success.

Furthermore, even if a *prima facie* case of obviousness has been established with respect to the applicants' composition as previously claimed, which applicants dispute herein, an applicant can rebut a *prima facie* case of obviousness by showing that the particular range, or concentration, achieves unexpected results. MPEP § 2144.05 (III). The non-obviousness of applicants' claimed composition is illustrated in the unexpected results of the 20mg prednisolone with the anti-bacterial compound.

Unexpected Results of the Claimed Dosages demonstrate non-obviousness

As outlined in the response submitted April 8, 2008, which response is incorporated in its entirety by reference herein, the claimed composition provides increased anti-inflammatory efficacy while unexpectedly not increasing immunosuppressive side effects as compared to compositions comprising less prednisolone. The as-filed Specification outlines exemplary manners in which this efficacy is unexpectedly improved. In Example 4, the Specification describes experimental results stating:

> "total leukocyte counts in blood is lower in cows treated with [the antibacterial agent] cephapirin and prednisolone (group 3) than in cows treated with cephapirin alone, but not different from total leukocyte counts in blood from not treated cows." *See, e.g.,* as-filed application, page 12, lines 26-30, emphasis added.

As described in the foregoing passage, administration with both cephapirin and prednisolone was not different from those animals that were untreated or did not receive the composition. Based on the references relied upon by the Examiner, one of ordinary skill in the art would not have expected this. For example, Lohuis' teaches contrasting results, to wit, a substantial increase in leukocyte counts of prednisolone as compared to non-treated animals. *See, e.g.,* Lohuis, Figure 3, and Final Office Action, page 3. Applicants respectfully note that the language of claims 1-3 and 7 are consistent with these unexpected results. More particularly, the language of new claim 11 specifically outlines the methods and that achieved these unexpected results.

Example 4 of the as-filed Specification provides another way in which the efficacy of applicants' claimed composition is unexpectedly improved. Example 4 states, in part,

> "[a]t 24 h after endotoxin infusion the chemotaxis of blood PMNs was higher in group 3 than in group 1 or 2. (Table 2 and FIG. 4). 20 mg prednisolone seems to increase the ability of PMN to migrate into the udder since chemotaxis of blood PMNs increases after intramammary infusion of cephaprin and 20 mg of prednisolone."
> As-filed Specification at 13, lines 21-26.

Thus, applicants' claimed composition provides significantly improved chemotaxis of PMNs (polymorphonuclear leukocytes), and as indicated above by the Specification, increases the ability of the PMNs to migrate into the udder. *Id.* This significant improvement is further illustrated in Figure 4. Applicants respectfully note that the language of new claim 10 is consistent with these unexpected results.

Applicants submit that none of references relied upon by the Examiner when combined and/or considered as a whole teaches or suggests a composition as presently claimed, nor do the combined references teaches or suggests that a person of ordinary skill in the art would have expected the results of applicants' composition. For example, and as described in more detail in the response submitted April 8, 2008, Farnsworth teaches the effects of a prednisolone/anti-bacterial composition on a yeast infection, stating that the mammary glands in the study were not infected with bacteria. Farnsworth, page 348, col. 1, lines 12-13. Thus, at most, Farnsworth teaches and/or suggests that a 10 mg prednisolone composition including an anti-bacterial compound can be used to treat a yeast infection.

Additionally, and as described in more detail in the Response of April 8, 2008, Lohuis discusses the effects of a 40 mg unit dose of prednisolone in *E. coli* endotoxin induced mastitis, where no antibacterial agent was administered. Lohuis, page 248, column 1, lines 48-51. While Lohuis suggests that use of 40 mg of prednisolone may increase leukocyte counts, Lohuis does not teach or suggest that higher dosages of prednisolone with an antibacterial compound can provide increased anti-inflammatory efficacy while not increasing immunosuppressive side effects. Furthermore, the different experimental results obtained by applicants using both prednisolone and an antibacterial compound, suggests that using higher prednisolone dosages with an anti-bacterial compound does not have similar effects as the administration of prednisolone as taught in Lohuis.

Applicants additionally submit that the presently amended claims 1-3 and 7 are not obvious as the claim language therein is more than adequately distinguished from both Farnsworth and Lohuis. Claims 1, 3, and 7 have been amended to recite, in part, wherein the increased anti-inflammatory efficacy while not increasing immunosuppressive side effects may be determined by displaying a similar leukocyte count upon administration to the non-human mammal when administered intramammarily." Nowhere in Farnsworth or Lohuis is there any suggestion that the increased anti-inflammatory efficacy may be determined by a similar leukocyte count. In fact, Lohuis' teachings directly contrast and teach away from this claim element.

In view of the foregoing, applicants submit that claims 1-3 and 7 are not obvious over Farnsworth and Lohuis. Reconsideration and withdrawal of the 35 U.S.C. § 103(a) rejections is respectfully requested.

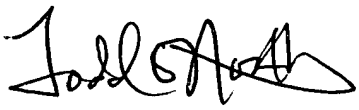
2. Claims 4-6 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Farnsworth in view of Lohuis and in further view of Hornish et al. (Current Topics in Med. Chem. July 2002 (2):717-731; hereinafter 'Hornish'). Applicants respectfully traverse the rejection as follows.

Claims 4-6 directly or indirectly depend from claim 1, and therefore, are patentable over the references relied upon by the Examiner for at least the same reasons as claim 1. Reconsideration and withdrawal of the rejection is respectfully requested.

CONCLUSION

In light of the above amendments and remarks, the application should be in condition for allowance. If questions remain after consideration of the foregoing, or if the Office should determine that there are additional issues which might be resolved by a telephone conference, the Office is kindly requested to contact applicants' attorney at the address or telephone number given herein.

Respectfully submitted,



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Enclosures: Petition for 3-month Extension of Time
Request For Continued Examination Under 37 CFR 1.114

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Document in ProLaw